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Comparison of the results of early and elective endoscopic retrograde cholangiopancreatography in patients with mild cholangitis

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ABSTRACT

Aims: The optimal duration of endoscopic retrograde cholangiopancreatography (ERCP) in patients with mild cholangitis and when it should be performed is unclear. This study aimed to compare the results of patients with mild cholangitis who underwent early and elective ERCP.

Methods: This study was designed as a retrospective study to compare the results of elective (time from admission to ERCP>72 h) and early (time from admission to ERCP≤72 h) ERCP in patients with mild cholangitis according to the Tocyo 18 (TC18) guideline. The study included patients with naive papillae and mild cholangitis who underwent ERCP between February 2019 and 2023 at a single tertiary center's gastroenterology clinic.

Results: A total of 432 mild cholangitis patients were included in our study. The mean age and ASA score of the elective ERCP group was slightly higher than the other group (respectively, p=0.039 and p=0.025). No significant difference was found between the two groups in terms of technical and clinical success, mortality, ERCP-related adverse events, organ failure and intensive care unit admission. Length of hospital stay (LHS) was significantly (p<0.001) higher in the elective group compared to the early group.

Conclusion: Our study showed that in patients with mild cholangitis with uncertain optimal ERCP time, ERCP in the early or elective period had no significant effect on mortality and other adverse outcomes, but ERCP in the early period shortened the patients' LHS duration.

Keywords: ERCP, mild cholangitis, mortality, pancreatitis

INTRODUCTION

Acute cholangitis is a medical condition caused by obstruction of the bile ducts for various reasons.[1] Although causes such as stricture, malignancy and parasites are involved in the etiology, the most common cause is bile duct stones.[2] Acute cholangitis is fatal in 5-10% of cases if not diagnosed and treated in time.[3]

Depending on the severity of the disease, treatment for acute cholangitis consists mainly of antimicrobial therapy and biliary decompression.[4] Biliary decompression is performed by endoscopic retrograde cholangiopancreatography (ERCP) or interventional radiological drainage. The optimal duration of ERCP in patients with acute cholangitis is still unclear. In a study investigating the optimal duration of ERCP in patients with acute cholangitis, it was reported that the duration of hospitalisation increased and some additional adverse outcomes occurred in patients undergoing ERCP after 48 hours.[5] Another study suggested that there was no significant difference in adverse outcomes in patients with non-severe acute cholangitis who underwent emergency or elective biliary drainage.[6] The most comprehensive guideline on this topic is the Tokyo (TC) 18 guideline revised in 2018.[7] According to this guideline, the diagnosis of acute cholangitis is based on systemic inflammation, cholestasis and imaging findings and is divided into 3 categories as severe, moderate and mild. While urgent biliary drainage is recommended for patients with severe cholangitis and early biliary drainage is recommended for patients with moderate cholangitis, antibiotic treatment or biliary drainage is recommended for patients with mild cholangitis. However, in this guideline, it is unclear when biliary drainage should be performed in patients with mild cholangitis.[7]

In the literature, studies that included patients with mild to moderate cholangitis have evaluated the optimal duration of ERCP[8] but we could not find studies that included patients with mild cholangitis only. In this

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study, we aimed to compare the results of patients with mild cholangitis who underwent early and elective ERCP.

METHODS

Ethics

Ethical approval was obtained from the Yıldırım Beyazıt University Faculty of Medicine Clinical Researches Ethics Committee (Date: 26.05.2021, Decision No: 56) and the study was conducted in accordance with the tenets of the Declaration of Helsinki.

Study Design and Patients

This study was designed as a retrospective study to compare the results of elective (time from admission to ERCP>72 h) and early (time from admission to ERCP≤72 h) ERCP in patients with mild cholangitis. The study included patients with naive papillae and mild cholangitis who underwent ERCP between February 2019 and 2023 at a single tertiary center's gastroenterology clinic. Using electronic medical records and the endoscopy database, we retrospectively analysed data from consecutive patients who underwent ERCP for mild cholangitis. Except for the diagnosis of mild cholangitis, patients with surgically altered anatomy (Billroth 2 gastrectomy or Roux-en-Y anastomosis), those under 18 years of age, those who had undergone sphincterotomy were excluded from the study. Patients with missing records and data were also excluded from the study.

ERCP Procedures

Antibiotic treatment and fluid resuscitation were given to all enrolled patients before the procedure. All ERCPs were performed using a lateral scope (TJF 190; Olympus Optical, Tokyo, Japan) by an experienced endoscopist who performs >800 therapeutic ERCPs per year. Patients were sedated with propofol and midazolam by anestegiologist. Standard biliary cannulation was performed using a guide wire and sphincterotome. Alternative techniques such as double guidewire and precut were used when selective biliary cannulation could not be achieved with this method. All patients were hospitalised for at least 24 hours after the procedure.

Definitons

Acute cholangitis was diagnosed and graded according to the TG18 guidelines for acute cholangitis[9]. Patients who underwent ERCP within 72 hours of admission were classified as having undergone an "early period", while patients who underwent ERCP beyond 72 hours of admission were classified as having undergone an "elective period". Comorbidity scores were calculated for the patients in the study using the Charlson Comorbidity Index (CCI)[10]. American Society of Anesthesiologists' Physical Status (ASA-PS) score[11] was divided into two groups: below and above 2 points. Weekends were defined as Saturday, Sunday and public holidays in Turkey. Night time was defined as 5 pm to 8 am, during which time there was no outpatient service in our hospital. Technical success was defined as successful decompression of the bile duct. Clinical success was defined as improvement in symptoms of cholangitis and laboratory findings such as CRP and white blood cell count improved within 7 days of ERCP. ERCP-related adverse events (AEs) in all patients after the procedure were defined according to international consensus criteria.[12] Organ failure was defined as hypotension requiring vasopressors, need for mechanical ventilation, or acute kidney injury (1.5-fold increase in serum creatinine from baseline or need for dialysis) persisting for more than 48 hours.[13]

Study Outcomes

The primary outcomes included technical success, clinical success, in-hospital mortality, intensive care unit (ICU) admission, organ failure and early adverse events associated with ERCP. The secondary outcome of this study was the length of hospital stay (LHS) between the two groups.

Statistical Analysis

In our study, the data were analysed using SPSS 25 (Armonk, NY: IBM Corp.) software. Mean, standard deviation, median (quartiles), frequency and percentage statistics were used to express numerical variables. Normality assessment was performed with Kolmogorov-Smirnov and Shapiro-Wilk tests. Student-t and Mann Whitney U tests were used to analyse numerical variables. Chi-square (Pearson, Yates and Fisher's) tests were used to analyse categorical variables. In the analyses of the relationship between numerical variables and ERCP groups, two-tailed correlation coefficients and phi coefficients were used for categorical variables. The significance level was set at 0.05 for all analysis.

RESULTS

A total of 432 mild cholangitis patients were included in our study. Although the age of the elective ERCP group was slightly higher than the other group (p=0.039), the gender distribution was similar between both groups (p=0.824). The high number of patients with Charlson index greater than two in the elective patient group did not lead to a significant result (p=0.168), whereas the high number of patients with ASA score greater than two led to a significant result (p=0.025) in this group. Time of hospital admission was concentrated during working hours in the early ERCP group (60.6%), while in the elective ERCP group it was mostly (37.6%) during holidays (p<0.001). Other variables and detailed results of the variables are presented in Table 1.

Table 1. Basic characteristics

Variables	All cases	Early ERCP (≤72 hours, n=203)	Elective ERCP (72 hours<, n=229)	p
Age	62.1±16.2	60.4±17.2	63. 6±15	0.039
Sex				
Male	211 (48.8)	98 (48.3)	113 (49.3)	0.824
Female	221 (51.2)	105 (51.7)	116 (50.7)	
Charlson comorbidity index				
<=2	221 (51.2)	111 (54.7)	110 (48)	0.168
>2	211 (48.8)	92 (45.3)	119 (52)	
ASA-PS score				0.025
<=2	351 (81.3)	174 (85.7)	177 (77.3)	
>2	81 (18.8)	29 (14.3)	52 (22.7)	
History of cholecystectomy	61 (14.1)	31 (15.3)	30 (13.1)	0.518
Time of hospital admission				
Working hours	188 (43.5)	123 (60.6)	65 (28.4)	<0.001
Night time	155 (35.9)	77 (37.9)	78 (34.1)	
Weekends	89 (20.6)	3 (1.5)	86 (37.6)	
Etiology of acute cholangitis				0.227
Bile duct stones	368 (85.2)	177 (87.2)	191 (83.4)	
Malignancy	22 (5.1)	14 (6.9)	12 (5.2)	
Benign structure	17 (3.9)	6 (3)	14 (6.1)	
Others	25 (5.8)	6 (3)	12 (5.2)	
Laboratory datas				
WBC	9.5 (7.26 - 12.1)	9.5 (7.17 - 12.1)	9.3 (7.3 - 11.9)	0.989
Crp	29.4 (13.8 - 78.2)	29 (13.2 - 74.3)	31.8 (14.1 - 82)	0.667
Tbil	3.6 (2.1 - 5.4)	3.7 (2.3 - 5.6)	3.5 (1.9 - 4.9)	0.061
GGT	449 (249.5 - 684)	446 (267 - 699)	457 (235 - 681)	0.736

Numerical variables with normal distribution are presented as mean±standard deviation, skewed distributions as median (Q1-Q3), and categorical variables as n(%).

It was concluded that technical and clinical success did not vary according to the duration of ERCP (p=0.455 and p=0.872 respectively) and that adverse events were not related to the duration of ERCP. ICU admission increased slightly in the elective ERCP group, but did not reach significance (p=1.00). Median LHS was significantly (p<0.001) higher in the elective group compared to the early group, while hospital stay after ERCP was almost significantly lower in the elective group (p=0.057). The results of the analyses are presented in Table 2.

The associations of variables with categorised ERCP duration were also analysed. Especially LHS was observed to increase in the elective ERCP group (rpb=0.449 and p<0.001). However, similar relationships to the results of univariable analyses were observed for other variables (Figure 1, Figure 2).

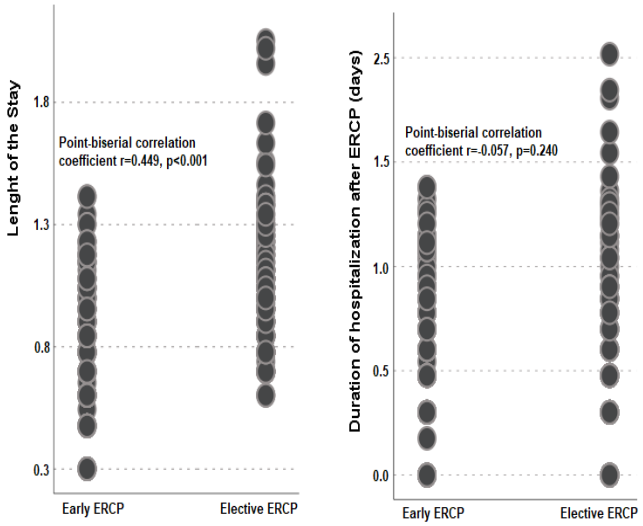

Figure 1. Scatter of logarithmic values of length of stay and duration of hospitalization after ercp variables with ercp duration

Table 2. Analysis of variables according to ERCP time

Variables	Early ERCP (≤72 hours, n=203)	Elective ERCP (72 hours<, n=229)	p
Technical success	201 (99)	224 (97.8)	0.455*
Clinical success	188 (92.6)	213 (93)	0.872
Adverse events associated with ERCP			
Pancreatitis	26 (12.8)	35 (15.3)	0.461
Bleeding	7 (3.4)	6 (2.6)	0.825**
Perforation	0 (0)	4 (1.7)	0.126*
Organ failure	2 (1)	2 (1)	1.00*
Admission to intensive care unit	5 (2.5)	6 (2.6)	1.00**
In-hospital mortality	2 (1)	2 (1)	1.00*
Length of stay, days	6 (4-6)	9.5 (7-13)	<0.001
Duration of hospitalization after ERCP, days	4 (2-6)	3 (1-5)	0.057

Variables are presented as n (%). *: Fisher Exact test, **: Yates correction

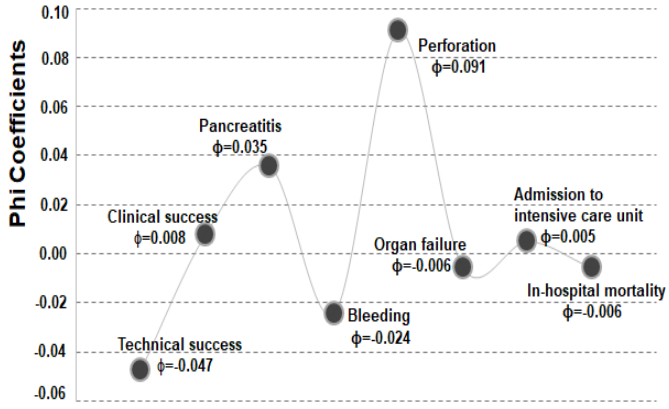

Figure 2. Scatter of phi coefficients between ERCP duration and categorical variables

DISCUSSION

This study showed that there was no significant difference between early (first 72 hours) and elective ERCP (after 72 hours) in terms of mortality, organ failure, intensive care unit stay, ERCP-related complications, technical and clinical success in patients with mild cholangitis. Another important finding of the study is that patients with mild cholangitis who underwent early ERCP had a significantly shorter LHS.

The controversy surrounding the optimal duration of ERCP in patients with acute cholangitis is still ongoing. In a retrospective study published in 2017, the duration of ERCP in patients with acute cholangitis was divided into two groups according to the time before and after 48 hours. ICU admission and LHS were significantly more common in patients who underwent late ERCP. When the same study evaluated the groups according to 72-hour duration, hypotension requiring vasopressors was also found significantly more frequently in the late group patients. However, this study included all grades of acute cholangitis together.[5] The findings and hypotheses of a recent retrospective study by Huang et al.[14] are interesting. In this study, subgroup analyses were performed in all patients with severe, moderate and mild cholangitis. There was no significant difference in 30-day mortality and ICU admission rates in patients with mild cholangitis when evaluated in both the 24-hour and 48-hour groups, whereas LHS was found to be significantly shorter in the early groups.[14] In another study, patients with non-severe cholangitis were defined and compared as emergency and elective groups according to the first 12 hours and beyond. According to this study, no significant difference was found between the groups in any parameter including mortality, organ failure, ICU admission and LHS.[6] A review of published guidelines, in addition to studies in the literature, shows that the optimal duration of ERCP is controversial. The American Society of Gastrointestinal Endoscopy (ASGE) guideline 2021 evaluated the association of acute cholangitis with adverse outcomes, primarily in patients with severe and moderate cholangitis, and suggested that ERCP performed within the first 48 hours significantly reduced 30-day mortality and length of hospital stay.[15] The European Society of Gastrointestinal Endoscopy (ESGE) recommended that severe cholangitis patients should be performed within the first 12 hours, moderate cholangitis patients should be performed within 48-72 hours, while no time recommendation was made for patients with mild cholangitis and elective ERCP was recommended.[16] The results of three recent meta-analyses show that the discussion about the optimal timing of ERCP is mainly focused on 24 hours and 48 hours, based on data analysis of significant outcomes in their respective time frames. However, these three trials reported that the optimal timing of ERCP did not affect survival outcomes in patients with acute cholangitis of different severity - mild, moderate and severe.[17-19] We think that patients with acute cholangitis should be analysed in separate groups according to the severity of cholangitis in order to investigate the optimal duration of ERCP. In addition, the common finding of all these studies is that the LHS of patients who underwent ERCP in the early period is shorter.[17-19] In our study, LHS was found to be significantly shorter in patients who underwent ERCP in the early period, which is similar to the literature.

In our study, the fact that age and ASA score were significantly higher in the elective group, despite the small difference, suggests that these patients may be mainly due to prolonged preoperative anaesthetic

preparation. However, the fact that there was no significant difference in the primary outcome parameters between the elective group and the early group, despite the higher age and ASA score, is another notable finding of our study. There was no significant difference between the two groups in terms of ERCP-related complications, mortality, organ failure and admission to ICU. Perforation was seen in 4 patients in the elective group and only one of these patients was operated on and died in the follow-up due to prolonged ICU hospitalisation and non-cholangitis infection. In the other patients, a metal fully covered stent was placed during the procedure and the patients were discharged after follow-up. However, there was no significant statistical difference between the groups in this study.

Limitations

The most important limitation of our study is that it was retrospective and single-centre. Moreover, the relatively small number of patients included was a further limitation. Finally, the fact that only in-hospital mortality was assessed in the mortality factor and the lack of mortality data at 1 month or later can also be considered as a limiting aspect of the study.

CONCLUSION

Our study showed that in patients with mild cholangitis with uncertain optimal ERCP time, ERCP in the early or elective period had no significant effect on mortality and other adverse outcomes, but ERCP in the early period shortened the patients' LHS duration. However, large and multicentre studies are needed to clarify the definitions of duration in the literature and the optimal duration of ERCP in patients with mild cholangitis.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Yıldırım Beyazıt University Faculty of Medicine Clinical Researches Ethics Committee (Date: 27.05.2021, Decision No: 56).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contrubitions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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